

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings of claims in the application:

Listing of Claims:

1-109. (canceled)

110. (Currently amended) A method for designing an oligonucleotide sequence having a selected duplex stability comprising:

- a) providing an oligonucleotide having a sequence of N bases and N-1 neighboring base pairs, wherein said oligonucleotide comprises at least one modified base selected from the group consisting of a universal base, unsubstituted and 3-substituted pyrazolo[3,4-d]pyrimidines and 5-substituted pyrimidines; and
- b) calculating the duplex stability of said oligonucleotide using an algorithm applying a nearest-neighbor model for duplex formation thermodynamics for each of the N-1 neighboring base pairs, each nearest neighbor thermodynamic parameter defining a thermodynamic contribution of two corresponding neighboring bases, optionally repeating steps a)-b) to obtain a sequence having said selected duplex stability; and
- c) outputting the sequence to a user or a display.

111. (Currently amended) A method for designing an oligonucleotide sequence having a selected duplex stability comprising:

- a) providing an oligonucleotide having a sequence of N bases and N-1 neighboring base pairs, wherein said oligonucleotide comprises at least one modified base selected from the group consisting of a universal base, unsubstituted and 3-substituted pyrazolo[3,4-d]pyrimidines and 5-substituted pyrimidines; and a minor groove binder; and
- b) calculating a melting temperature (T_m) of said oligonucleotide using an algorithm applying nearest neighbor thermodynamic parameters for each of the N-1 neighboring base pairs, each nearest neighbor thermodynamic parameter defining a thermodynamic

contribution of two corresponding neighboring bases, optionally repeating steps a)-b) to obtain a sequence having said selected duplex stability; and

c) outputting the sequence to a user or a display.

112. (Previously presented) The method of any one of claims **110** or **111**, wherein said oligonucleotide sequence is derived from a database source.

113. (Previously presented) The method of claim **112**, wherein said database source is GENBANK.

114. (Previously presented) The method of any one of claims **110** or **111**, wherein said at least one modified base is a member selected from the group consisting of a base attached to an amino acid, a polyamide nucleic acid (PNA) and a locked nucleic acid sugar.

115. (Previously presented) The method of claim **114**, wherein said modified base is attached to PNA.

116. (Previously presented) The method of claim **114**, wherein said modified base is attached to a locked nucleic acid sugar.

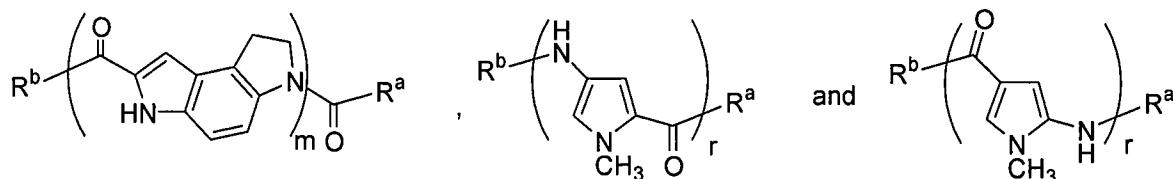
117. (Previously presented) The method of any one of claims **110** or **111**, wherein said oligonucleotide has an enhanced ability of mismatch discrimination, in comparison to unmodified nucleotides.

118. (Previously presented) The method of any one of claims **110** or **111**, wherein said at least one modified base is a member selected from the group consisting of a universal base, PPA, PPG, PPPA, PPPG, PU, PC, HOPU, HOBuU, HOBuC, (NH₂)₂PPPA, (NH₂)₂PPPAOH, (NH₂)₂BuPPPAOH, (NH₂)₂PPAI, and HOBuPPG.

119. (Previously presented) The method of claim **110**, wherein said oligonucleotide has attached to it one or more members selected from the group consisting of a minor groove binder, a fluorophore and a quencher.

120. (Previously presented) The method of claim **119**, wherein said oligonucleotide sequence has a minor groove binder attached thereto.

121. (Previously presented) The method of claim **111** or **120**, wherein said minor groove binder has a formula selected from the group consisting of:



wherein

the subscript m is an integer of from 2 to 5;

the subscript r is an integer of from 2 to 10; and

each R^a and R^b is independently a linking group to said modified oligonucleotide, H, OR^c, NR^cR^d, COOR^c and -CONR^cR^d wherein each R^c and R^d is selected from the group consisting of H, (C₁-C₁₂)heteroalkyl, (C₂-C₁₂)heteroalkenyl, (C₂-C₁₂)heteroalkynyl, (C₁-C₁₂)alkyl, (C₂-C₁₂)alkenyl, (C₂-C₁₂)alkynyl, aryl(C₁-C₁₂)alkyl and aryl.

122. (Previously presented) The method of claim **120**, wherein said minor groove binder is attached to the oligonucleotide via a quencher molecule.

123. (Previously presented) The method of any one of claims **110** or **111**, wherein said algorithm predicts the melting temperature (T_m) of said oligonucleotide with an accuracy of about +/- 2°C.

124. (Previously presented) The method of any one of claims **110** or **111**, wherein said method is applied to establish conditions for hybridization, renaturation, mapping

variations of base compositions of sequences or determination of sequence complexity and divergence.

125. (Previously presented) The method of any one of claims **110** or **111**, wherein said oligonucleotide is a capture probe in an array.

126. (Previously presented) The method of claim **115**, wherein said oligonucleotide has an enhanced ability of mismatch discrimination, in comparison to unmodified nucleotides.

127. (Previously presented) The method of claim **116**, wherein said oligonucleotide has an enhanced ability of mismatch discrimination, in comparison to unmodified nucleotides.